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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/250,056 02/12/99 MARKS

J 2307E-852

020350 HM22/0315  
TOWNSEND AND TOWNSEND AND CREW  
TWO EMBARCADERO CENTER  
EIGHTH FLOOR  
SAN FRANCISCO CA 94111-3834

EXAMINER

HELMS, J

ART UNIT

PAPER NUMBER

1642

DATE MAILED:

03/15/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
09/250,056

Applicant(s)

Marks et al

Examiner

Larry R. Helms Ph.D.

Group Art Unit

1642



☒ Responsive to communication(s) filed on 16 Jan 2001

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

☒ Claim(s) 1, 3-22, 34-44, 53, and 54 is/are pending in the application

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1, 3-22, 34-44, 53, and 54 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### **DETAILED ACTION**

1. Claims 1, 3-22, 34-44 and 53-54 are pending and under examination.  
Claim 1 has been amended.
2. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
3. The following office action contains some NEW GROUNDS of rejections.

### ***Oath/Declaration***

4. The Examiner acknowledges that a new oath is being executed, however, the oath or declaration is still defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is still defective because:

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, **as amended by any amendment** [emphasis added] specifically referred to in the oath or declaration.

### ***Information Disclosure Statement***

5. The references C40, B6, B7, and B8 were considered.

***Rejections Withdrawn***

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6. The rejection of Claims 1, 3-22, 34-44, and 53-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

***Response to Arguments***

7. The rejection of claims 3-13, 16-22, 34-44, and 53-54, under 35 U.S.C. 112, first paragraph, is maintained.

The response filed 1/16/01 has been carefully considered but has been deemed to be not persuasive. The response states that "The examiner is reminded that to be enabling under 112, first paragraph, a patent must contain a description that enables one skilled in the art to make and use the claimed invention." and that some experimentation is necessary does not constitute lack of enablement (See page 5). As stated in the previous Office Action, "The statement is correct that enablement encompasses making and using the claimed invention. The rejection under 112, first paragraph was made due to a lack of enablement provided by the specification, specifically it is known in the art how to make (1) substitutions within an antibody sequence, (2) calculate 70% identity of one sequence to another, and (3) produce a protein that contains one or two CDRs, however, applicant has not demonstrated how to use such proteins. It is unclear that an antibody that contains one, two, or three CDR would bind antigen as claimed. In addition, the specification does not enable the myriad of antibodies encompasses by claim 4 which recites an antibody that is 70% sequence identity with SEQ ID NO:1 or 2 that would bind to the c-erbB2 on

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cells at 10 mM. At this concentration there would be significant cross reactivity with many antibodies and these antibodies would not function as claimed in claim 1. Moreover, it is not clear if an antibody that comprises at least 10 contiguous amino acids (which can be framework residues) from the polypeptide as set forth in SEQ ID NO:1 or 2 would bind specifically to the c-erbB2 receptor as claimed in claim 16. As stated in the rejection in the previous Office Action the art of record demonstrates it is unpredictable how to use the claimed antibodies as broadly claimed. The response set forth on pages 4-6 does not address the unpredictability in the art as evidenced by Rudikoff et al, Panka et al, Adair et al, and Amit et al.” In addition, the response states that the antibodies of claims 6-13, 19-20, and 53-54 are antibodies which are directed to c-erbB2 binding antibodies in which one, or two or three CDRs are selected from the recited sequences” (see page 5 of response). In response to this argument, the statement is true and the claims encompass antibodies which do not contain a full set of 6 CDRs of SEQ ID NO:1 or 2 and as such would not bind antigen. In addition, because of the limitation of binding affinity of 10mM, as stated above one skilled in the art would realize that at this concentration many antibodies which may not be “specific” for the receptor would bind.

8. The rejection of Claims 1, 14, 15, 34-38, and 53-54 under 35 U.S.C. 103(a) as being unpatentable over Maier et al (Cancer Res. 51:5361-5369, 1991) and further in view of Bird et al (Science 242:423-426, 1988) is maintained and made again.

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The response filed 1/16/01 has been carefully considered but is deemed not to be persuasive. The response states Maier et al discloses tetramers and includes the constant region (see page 7 of response) and "There is no teaching or suggestion in Bird et al regarding an anti-c-erbB2 antibody" (see page 8). In response to these arguments, Bird et al teaches the advantage of single chain antibodies because of their small size (see page 426) for therapy. In addition, it would have been obvious to produce a single chain antibody from the antibody of Maier et al which is directed at the therapeutic target c-erbB2 because of the advantages of the small size and advantages in imaging and therapy in cancer as taught by Bird et al (see page 426 in Bird).

### *Summary*

9. No claims are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.
11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

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Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Larry R. Helms Ph.D.

  
SHEELA HUFF  
PRIMARY EXAMINER